Remarks

Claims 20, 21, 27 and 28 are currently amended to specifically recite topical application of the claimed agent to a region of skin exhibiting fine lines and clinical wrinkles. Support for this amendment is found, *inter alia*, in originally-filed Claims 10 and 11.

Claim 20 has been further amended to recite a particular type of damaged dermal or epidermal tissue to which the claimed compound is applied – namely, normal photodamaged tissue. Support for this amendment is found in Paragraph [0021] of the Application.

The imidazoquinoline amine derivatives claimed in currenty-amended Claim 34 are taught in van Galen *et al.*, "1H-imidazo [4,5-c] quinolin-4-amines: novel non-xanthine adenosine antagonists," *J. Med. Chem.* Vol. 34, No. 3, pp. 1202-6 (1991). *See*, in particular, Table 1 at page 1204. The disclosure of the van Galen article is incorporated by reference in its entirety in Paragraph [0019] of the Application.

New matter is not added by the above amendments.

A1. Currently-Amended Claims 20, 21, 27 and 28 Are Not Anticipated by Stockfleth

Previously presented Claims 20, 21, 27 and 28 stand rejected as anticipated by Stockfleth under 35 USC § 102(b). For the following reasons, Applicants respectfully traverse and request reconsideration and withdrawal of these rejections.

As currently-amended, each of independent Claim 20 and its dependent Claim 21 is now directed a method of topically applying a dermatocosmetic composition comprising an immunomodulatory compound of a specified structure that is capable of attracting macrophage cells and thereby "inducing an immune cytotoxic response in a section of damaged dermal or epidermal tissue of a patient exhibiting fine lines and clinical wrinkles." (emphasis added.)

Currently-amended independent Claim 27 and its dependent Claim 28 each add a similar limitation. Both of these claims are now directed to a method for topically applying a dermatocosmetic composition comprising 1-isobutyl-1H-imidazo [4,5-c] quinolin-4-amine to skin exhibiting fine lines and clinical wrinkles and thereby identifying whether that region of skin is precancerous.

Applicants respectfully submit that application of dermatocosmetic composition to skin exhibiting fine lines and clinical wrinkles is a required claim element that is not taught by Stockfleth. As the Office Action recognized, actinic keratosis is a pathological condition that is distinct from cosmetic skin conditions of fine lines and clinical wrinkles.

Claims 27 and 28 as currently amended are directed to diagnostic methods, and not methods of treatment. Applicants respectfully submit that diagnosis and treatment are patentably-distinct subject matter not taught in Stockfleth.

In light of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the rejections of Claims 20, 21, 27 and 28 under 35 USC § 102(b) based on Stockfleth.

A2. Currently-Amended Claim 29 Is Not Rendered Obvious by Stockfleth

Claim 29 stands rejected as obvious based on the teachings of Stockfleth under 35 USC § 103(a). Claim 29 depends from currently-amended Claim 28 and thus incorporates the limitation added to that claim – application of dermatocosmetic composition to skin exhibiting fine lines and clinical wrinkles. As discussed in Section A1, this limitation is not otherwise taught or suggested by Stockfleth. For this reason, Applicants respectfully request withdrawal of the rejection of Claim 29 under 35 USC § 103(a) based on Stockfleth.

B. Currently-Amended Claims 20 and 21 Are Not Obvious in Light of Maibach

Claims 20 and 21 as previously presented stand rejected as obvious under 35 USC § 103(a) based on the teachings of Maibach (US Patent Application 10/178,082).

Claim 20 has now been amended to add limitations not otherwise taught or suggested by Maibach – application of dermatocosmetic composition to a section of skin exhibiting fine lines and clinical wrinkles where the section of skin is not being treated for viral infection or skin cancer. As an initial matter, Applicants respectfully note that nowhere does the Maibach application mention fine lines or wrinkles. As discussed in Paragraph 15 of the Affidavit of Neil A. Swanson, M.D., submitted pursuant to 37 C.F.R. § 132 and now of record, the sole reference to imiquimod in Maibach is with respect to the treatment of warts. In Paragraph 15 of his Affidavit, Dr. Swanson explains that warts are caused by viral infection, specifically by the papilloma virus. Claim 20 now specifically directed to topical application of the recited compound to skin exhibiting fine lines and clinical wrinkles that is not being treated for viral infection.

Claim 21 depends from amended Claim 20 and thus incorporates this same limitation.

For the above reasons, Applicants respectfully request withdrawal of the rejections of Claims 20 and 21 under 35 USC § 103(a) based on Maibach.

C. Previously-Presented Claims 33 and 34 are Enabled

Previously Claim 33 and 34 stand rejected for failing to meet the requirements of enablement under 35 U.S.C. §112, first paragraph. As discussed in the first paragraph of the Remarks, Claim 34 is currently amended. For the following reasons, Applicants respectfully traverse the rejection of these claims and request reconsideration and withdrawal of these rejections.

There are eight *Wands* factors for determining whether the enablement requirement has been met. Among these is the breadth of the claims. Previously-presented Claim 33 and currently-amended Claim 34 are not overly-broad in scope.

To the contrary, the imidazoquinoline amine derivatives claimed in previously-presented Claim 33 have two substituents, R_1 and R_2, each of which is selected from a Markush group of four members. Previously-presented Claim 33 is thus directed to sixteen specifically-described imidazoquinoline amine derivatives:

	R_1	R_2
1	Hydrogen	Hydrogen
2	Hydrogen	Amine (NH_2)
3	Hydrogen	Chloride
4	Hydrogen	Phenoxy
5	Acetyl	Hydrogen
6	Acetyl	Amine (NH_2)
7	Acetyl	Chloride
8	Acetyl	Phenoxy
9	n-Butyl	Hydrogen
10	n-Butyl	Amine (NH_2)
11	n-Butyl	Chloride
12	n-Butyl	Phenoxy
13	Benzyl	Hydrogen
14	Benzyl	Amine (NH_2)
15	Benzyl	Chloride
16	Benzyl	Phenoxy

Similarly, currently-amended Claim 34 is directed to fifteen specifically-described imidazoquinoline amine derivatives. The substituents of these derivatives are each selected, respectively, from Markush groups consisting of five members (R_1) and three members (R_2):

	R_1	R_2
1	Hydrogen	Hydrogen
2	Hydrogen	Phenyl
3	Hydrogen	Cyclopentyl
4	Phenyl	Hydrogen
5	Phenyl	Phenyl
6	Phenyl	Cyclopentyl
7	Cyclopentyl	Hydrogen
8	Cyclopentyl	Phenyl
9	Cyclopentyl	Cyclopentyl
10	(R)-1-methyl-2-phenylethyl	Hydrogen
11	(R)-1-methyl-2-phenylethyl	Phenyl
12	(R)-1-methyl-2-phenylethyl	Cyclopentyl
13	(S)-1-methyl-2-phenylethyl	Hydrogen
14	(S)-1-methyl-2-phenylethyl	Phenyl
15	(S)-1-methyl-2-phenylethyl	Cyclopentyl

At Page 5, the Office Action states that the imidazoquinoline amine derivatives recited as claim element (a) in each of previously-presented Claim 33 and currently-amended Claim 34 are "never disclosed to possess toll-like receptor (TLR) activity, interferon induction, or any cytotoxic, antiviral or antitumor activity." These claims do not require that the recited imidazoquinoline amine derivatives have specific type(s) of biological activity. Instead, these claims are directed to method for treating fine lines or clinical wrinkles by application of a discrete subset of imidazoquinoline amine derivatives having a specific, limited number of substituents at two positions.

Each claim must be construed and examined as presented. Here, Claims 33 and 34 are directed to separate distinctly-claimed embodiments, other than imiquimod. Applicants respectfully submit that the rejection of previously-presented Claims 33 and 34 improperly reads limitations from the specification into the claims. *See*, § MPEP 2111.01, Part II. The limitation being read into the claims is that the imidazoquinoline amine derivatives claimed by reference to particular formulae act in a specific way. In this regard, at page 6, the Office Action notes the absence of working examples other than imiquimod. Applicants respectfully submit that where only a single embodiment is disclosed, the claims must not be construed as being limited to that embodiment. *See, e.g., Liebel-Flarsheim Co. v. Medrad Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004).

Applicants also respectfully note that it is a well-established tenet of the patent law that a scientific theory is not a requirement of patentability. *Newman v. Quigg*, 877 F.2d 1575, 1581-82 (Fed. Cir. 1989). According to *Newman*, it is not required that the inventors correctly set forth, or even know, how or why the invention works. *Id.*

In addition, Applicant's respectfully submit that raising enablement issues for the first time in a final Office Action is inconsistent with the principles of compact prosecution and the standards for examination set forth in MPEP § 2164.04. In accordance with

MPEP § 2164.04, if an enablement rejection were appropriate it should be raised in a non-final Office Action. Consistent with this Section, the Examiner should also communicate to the Applicants claim limitations that would render the rejected claims enabled. For this further reason, Applicant's respectfully request reconsideration of the enablement rejection of the last Office Action.

D. Applicants Conceived and Reduced to Practice the Invention of Treating Clinical Wrinkles and Fine Lines with Imiquimod Prior to the Earliest Date of Constructive Reduction to Practice by Miller et al.

Claims 11 – 17, 19 – 21 and 31 stand rejected under 35 USC § 102(e) as being anticipated by US Application Serial No. 10/799,999 to Miller *et al*. Claim 18 is rejected 35 USC § 103(a) as being unpatentable over Miller. Claims 30 and 32 also stand rejected 35 USC § 103(a) as being unpatentable over Miller in view of US Patent No. 4,689,338. The Miller Application claims priority to U.S. Provisional Patent Application No. 60/454,245, filed March 13, 2003. For purposes of this response, March 13, 2003 is taken to be the earliest date of constructive reduction to practice by Miller *et al.*

Both the Miller reference and the instant application describe methods for treating wrinkles by application of imidazoquinoline amines. Example 3 of Miller at Paragraphs [0067] – [0074] provides a prophetic example (*i.e.*, written in the present tense) of a method for treating facial wrinkles by application of a 5% cream of imiquimod at least daily. The instant application describes treatment of clinical wrinkles with imiquimod in Paragraphs [0009] and [0020].

Applicants respectfully note that while topical application of imiquimod is specifically claimed in the instant application including, for example, in dependent claim 13, Miller claims imidazoquinoline amines generally, but not imiquimod specifically. This is shown in the following table which reproduces pertinent sections of pending claims in both the Baumann / Welsh and Miller *et al.* applications:

Baumann / Welsh (10/627,944)	Miller *et al.* (10/799,999)
11. (Currently amended) A method for treating fine lines or clinical wrinkles on a section of aged skin or non-precancerous, normal photodamaged skin, said section of skin not being treated for viral infection or skin cancer, comprising topically applying an effective amount of a composition consisting essentially of (a) an imidazoquinoline amine derivative ...	8. A method of visibly reducing a human skin wrinkle comprising: topically applying to the human skin wrinkle an IRM compound in an amount and for a period of time sufficient to visibly reduce the wrinkle; wherein the IRM compound is an imidazoquinoline amine ...
13. (Currently amended.) The method of claim 11, wherein the imidazoquinoline amine derivative is 1-isobutyl-1H-imidazo [4,5-c] quinolin-4-amine, said derivative being present at a concentration of up to about 5% by weight of the total composition.	

As set forth in the Affidavit of Dr. Leslie Baumann submitted pursuant to 37 C.F.R. §1.131, Applicants submit that their use of imiquimod for the treatment of non-precancerous, normal photodamaged skin and aged skin predates March 13, 2003 – the date of earliest constructive reduction to practice by Miller *et al.*

The 1.131 Declaration of Dr. Baumann is submitted with this Response since the Miller reference was raised for the first time only in a Final Office Action.

Conclusion

For the above reasons, reconsideration and withdrawal of the rejections are respectfully requested. If the Examiner believes that an interview will expedite review, please contact undersigned counsel.

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Respectfully submitted,
Louis C. Paul & Associates, PLLC

Louis C. Paul
Registration No. 53,442

Louis C. Paul & Associates, PLLC
730 Fifth Avenue, 9th Floor
New York, NY 10019
Tel – (212) 659-7748
Fax – (212) 712-8840